DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Oncology (Oral – Bruton's Tyrosine Kinase Inhibitor) – Imbruvica Drug Quantity Management Policy – Per Rx
- Imbruvica® (ibrutinib tablets, capsules, and oral suspension – Pharmacyclics/Janssen)

REVIEW DATE: 07/03/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Imbruvica, a Bruton's tyrosine kinase inhibitor, is indicated for the following:[1]
- **Chronic lymphocytic leukemia (CLL)** or **small lymphocytic lymphoma (SLL),** in adults.
- **CLL** or **SLL,** with 17p deletion, in adults.
- **Graft-versus-host disease, chronic**, after failure of one or more lines of systemic therapy in adults and pediatric patients ≥ 1 year of age.
- **Waldenström macroglobulinemia,** in adults.

Dosing

For CLL, SLL, and Waldenström macroglobulinemia, the recommended dose of Imbruvica is 420 mg once daily (QD) until disease progression or unacceptable

toxicity.[1] It can be administered as a single-agent or in combination with other agents. For chronic graft-versus-host disease ≥ 12 years of age, the recommended dose of Imbruvica is 420 mg QD. For patients 1 to < 12 years of age, the recommended dose is 240 mg/m^2 QD (up to 420 mg QD), until disease progression, recurrence of an underlying malignancy, or unacceptable toxicity.

To manage adverse events, dose reductions/modifications to 280 mg QD or 140 mg QD may be needed for patients ≥ 12 years of age.[1] For patients 1 to < 12 years of age, modifications to 160 mg/m^2 or 80 mg/m^2 are recommended (potential doses are 70 mg, 140 mg, 210 mg, 280 mg QD using either the tablets or oral suspension). Similarly, dose reductions may be needed to manage drug interactions, as well as hepatic impairment.

Availability

Imbruvica is available as a 70 mg and 140 mg capsules and 140 mg, 280 mg, and 420 mg tablets.[1] Imbruvica is also supplied as a 70 mg/mL oral suspension in bottles containing 108 mL each.

Off-Label Dosing

Guidelines also support the use of Imbruvica for central nervous system lymphoma, hairy cell leukemia, mantle cell lymphoma, marginal zone lymphoma, and other B-cell lymphomas.[2-5] The recommended dose for mantle cell lymphoma, marginal zone lymphoma, and other B-cell lymphomas is 560 mg QD.[2] Dosing used for central nervous system lymphoma is up to 560 mg or 840 mg QD.[4,6-8] A dose of 420 mg QD is recommended for hairy cell leukemia.[5]

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Imbruvica. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
Imbruvica® (ibrutinib capsules, tablets and oral suspension)	70 mg capsules	30 capsules	90 capsules
	140 mg capsules	120 capsules	360 capsules
	140 mg tablets	30 tablets	90 tablets
	280 mg tablets	30 tablets	90 tablets
	420 mg tablets	30 tablets	90 tablets
	70 mg/mL oral suspension* (108 mL per bottle)	324 mL	972 mL

* Quantity limits for the Imbruvica oral suspension allow for a dose of 560 mg once daily, rounded up to the nearest bottle size; overrides are provided for patients who require doses of 840 mg once daily.

EXCEPTIONS TO THE QUANTITY LIMITS LISTED ABOVE ARE COVERED AS MEDICALLY NECESSARY WHEN THE FOLLOWING CRITERIA ARE MET. ANY OTHER EXCEPTION IS CONSIDERED NOT MEDICALLY NECESSARY.

CRITERIA

Imbruvica 70 mg capsules

1. If a patient requires a dose of 210 mg once daily, approve 90 capsules per dispensing at retail or 270 capsules per dispensing at home delivery.

Imbruvica 140 mg capsules

No overrides recommended.

Imbruvica 140 mg tablets

No overrides recommended.

Imbruvica 280 mg tablets

1. If the patient requires a dose of 560 mg once daily to treat central nervous system lymphoma, mantle cell lymphoma, marginal zone lymphoma, or other B-cell lymphomas, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.
   Note: Other B-cell lymphomas include diffuse large B-cell lymphomas, Acquired Immune Deficiency Syndrome (AIDS)-related B-cell lymphomas, post-transplant lymphoproliferative disorders, double/triple hit lymphoma, and high-grade B-cell lymphoma.

Imbruvica 420 mg tablets

1. If the patient requires a dose of 840 mg once daily to treat central nervous system lymphoma, approve 60 tablets per dispensing at retail or 180 tablets per dispensing at home delivery.

Imbruvica 70 mg/mL oral suspension

1. If the patient requires a dose of 840 mg once daily to treat central nervous system lymphoma, approve 432 mL per dispensing at retail or 1,080 mL per dispensing at home delivery.

REFERENCES

1. Imbruvica® tablets, capsules, and oral solution [prescribing information]. South San Francisco, CA and Horsham, PA: Pharmacyclics/Janssen; December 2024.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 5, 2025.
3. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2025. Search term: ibrutinib.
4. The NCCN Central Nervous System Cancers Guidelines in Oncology (version 1.2025 – June 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 5, 2025.
5. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 1.2025 – September 26, 2024). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 5, 2025.

6. Grommes C, Pastore A, Palaskas N, et al. Ibrutinib unmasks critical role of Bruton tyrosine kinase in primary CNS lymphoma. *Cancer Discov*. 2017;7:1018-1029.
7. Grommes C, Tang SS, Wolfe J, et al. Phase 1b trial of an ibrutinib based combination therapy in recurrent/refractory CNS lymphoma. *Blood*. 2019;133:436-445.
8. Soussain C, Choquet S, Blonski M, et al. Ibrutinib monotherapy for relapse or refractory primary CNS lymphoma and primary vitreoretinal lymphoma: final analysis of the phase II 'proof-of-concept' iLOC study by the Lymphoma study association (LYSA) and the French oculo-cerebral lymphoma (LOC) network. *Eur J Cancer*. 2019;117:121-130.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	New policy created to provide overrides to previously existing quantity limits.	07/12/2023
Annual Revision	No criteria changes.	07/17/2024
Annual Revision	The name of the policy was updated to "Oncology (Oral – Bruton's Tyrosine Kinase Inhibitor) – Imbruvica Drug Quantity Management Policy – Per Rx". Previously, the policy was named "Oncology – Imbruvica Drug Quantity Management Policy – Per Rx". There were no other changes to criteria.	07/03/2025